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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,123	02/03/2004	Corinna Sundermann	029310.53175US	7253

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,123	SUNDERMANN ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-52 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-52 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.000

DETAILED ACTION

1. Claims 1-52 are pending in the application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 47 and 50-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pain, does not reasonably provide enablement for alleviating (completely curing) pain and for treating/inhibiting all other disease conditions mentioned in instant claims 50-52. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858. F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant specification teaches inhibitory effect of instant compounds on the formaldehyde-induced nociception in rats (see example 52 on pages 60-62) as well as binding affinity for glycine-binding site of the NMDA receptor (see example 50 on pages 55-57). Based on these data, the instant compounds will have utility in treating but not alleviating (completely curing) pain since NMDA receptor antagonism is only one of the several other known mechanisms responsible for mediating pain. The binding data for glycine-binding site of the NMDA receptor shown in table 1 does not teach whether the instant compounds are agonists or antagonists at this site. It is well known in the art that the utility of any compound will be different (opposite) based on agonist versus antagonist activity at any receptor site. There is no teaching either in the specification or prior art whether glycine-site agonists or glycine-site antagonists are known in the prior art to have therapeutic utility in treating all disease conditions listed in instant claims 50-52 such as urinary incontinence, pruritus, diarrhea, parkinson's disease, osteoporosis, diabetes etc. There are no working examples present showing efficacy of instant compounds in known animal models of all disease conditions listed in instant claims 50-52 such as urinary incontinence, pruritus, diarrhea, parkinson's disease, osteoporosis, diabetes etc. The instant compounds of formula I encompasses several hundreds of thousands of compounds based on the values of variables R1-R8 and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of all disease conditions listed in instant claims 50-52 and hence their utility for treating these disease conditions.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 27, 36-42, 47, 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, page 71, lines 5 and 8, variables R1b and R2a are mentioned. However, these variables are not present in formula (I). Should it read R1 and R2?

In claims 27 and 36, the term ---producing----is vague. The applicants are suggested to change the term –producing--- to ---preparing--.

In claims 27 and 36, it is not clear whether compounds of formulae II, III and IV are reacted separately or simultaneously with trifluoroacetic acid to prepare compounds of formula I.

Claims 37-42 depend directly or indirectly upon claim 25 and further define the process of claim 25. However, claim 25 is directed to compounds and not process for preparing compounds and therefore, lack antecedal basis. An appropriate correction is needed.

In claim 47, the term –alleviating—is indefinite since the degree of alleviation (20%, 40%, 80% or 100%) is not defined and furthermore, it is not clear how this alleviation is being assessed in a mammal following in vivo administration of compounds of claim 1?

In claims 51 and 52, the term –inhibiting—is indefinite since the degree of inhibition (20%, 40%, 80% or 100%) is not defined and furthermore, it is not clear how this inhibition is being assessed in a mammal following in vivo administration of compounds of claim 1?

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-9, 11 and 15-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Borrione (J. Chem. Soc. Perkin Trans.).

Borrione discloses synthesis of optically active tetrahydroquinolines. The compounds 2a-d, 3a-d, 4a-d and 5a-d (see page 2246) disclosed by Borrione anticipate the instant claims when R3 represents cycloalkyl in the instant compounds of formula I.

7. Claims 1-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi (J. Combinat. Chem. 2000).

Kobayashi discloses preparation of tetrahydroquinoline derivatives. The compounds 8{1,1}, 8{2,3}, 8{2,1} and 8{3,4} disclosed (see scheme 2 on page 439) by Kobayashi anticipate the instant claims when R3 represents an alkyl group in the instant compounds of formula I.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Kobayashi (J. Combinat. Chem. 2001).

Kobayashi discloses preparation of tetrahydroquinoline derivatives. The compounds 14a, 14b, 14d and 14h (see page 199) disclosed by Kobayashi anticipate the instant claims when R3 represents an alkyl group in the instant compounds of formula I.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1-52 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Gerlach (U.S. Patent 6,699,877).

Gerlach discloses substituted 1,2,3,4-tetrahydroquinolines-2-carboxylic acid derivatives, a process for preparing these compounds, pharmaceutical compositions containing these compounds and methods of treating pain and other disease conditions using these compounds. The exemplified compounds (see examples 1-4, 6, 12, 59-64, 67 and 76) disclosed by Gerlach clearly anticipate the instant claims.

The applied reference has three common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-62 of U.S. Patent No. 6,699,877. Although the conflicting claims are not identical, they are not patentably distinct from each other because the values of variables R1 and R2 together disclosed in the cited patent are encompassed by the broader values of these variables in the instant application.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

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